Nil

File No. FDC/MA/23/000063
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(FDC Division)

Tele. No.: 011-23236965
Fax No. : 011-23236973

FDA Bhawan, Kotla Road
New Delhi-110002

Dated:

25 AUG 2023

To,

M/s. Exemed Pharmaceuticals,
Plot No. 133/1 & 133/2, G.I.D.C.,
Selvas Road, Vapi-396195, Gujarat.

Subject: **Permission to conduct Phase III clinical trial with the FDC of Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin 10mg + Metoprolol Succinate IP eq. to Metoprolol Tartrate (Extended Release) 50mg tablets (Vide protocol no. CT/2023/11, version no. 01, dated 28.04.2023)-regarding.**

Dear Sir,

With reference to your online application submitted in Form CT-21 on dated 10.03.2023 please find enclosed herewith the "permission to conduct clinical trial study of new drug" bearing no. **FDC-CT-06-39/2023** under the provision of Drugs and Cosmetics Act and Rules. The permission is subject to the conditions mentioned below.

Kindly acknowledge receipt to this letter and its enclosures.

Yours faithfully,

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

CONDITIONS OF PERMISSION

I. Clinical trial at each site shall be initiated after approval of the clinical trial protocol and other related documents by the Ethics Committee of that site, registered with the Central Licencing Authority under rule 8;

II. Where a clinical trial site does not have its own Ethics Committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the Ethics Committee of another trial site; or an independent Ethics Committee for clinical trial constituted in accordance with the provisions of rule 7:

   i. Provided that the approving Ethics Committee for clinical trial shall in such case be responsible for the study at the trial site or the centre, as the case may be:

   ii. Provided further that the approving Ethics Committee and the clinical trial site or the bioavailability and bioequivalence centre, as the case may be, shall be located within the same city or within a radius of 50 kms of the clinical trial site;

III. In case an ethics committee of a clinical trial site rejects the approval of the protocol, the details of the same shall be submitted to the Central Licensing Authority prior to seeking approval of another Ethics Committee for the protocol for conduct of the clinical trial at the same site;

IV. The Central Licencing Authority shall be informed about the approval granted by the Ethics Committee within a period of fifteen working days of the grant of such approval;

V. Clinical trial shall be registered with the Clinical Trial Registry of India maintained by the Indian Council of Medical Research before enrolling the first subject for the trial;

VI. Clinical trial shall be conducted in accordance with the approved clinical trial protocol and other related documents and as per requirements of Good Clinical Practices Guidelines and the provisions of these rules;

VII. Status of enrolment of the trial subjects shall be submitted to the Central Licencing Authority on quarterly basis or as appropriate as per the duration of treatment in accordance with the approved clinical trial protocol, whichever is earlier;

VIII. Six monthly status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Central Licencing Authority electronically in the SUGAM portal;

IX. In case of termination of any clinical trial the detailed reasons for such termination shall be communicated to the Central Licencing Authority within thirty working days of such termination;

X. Any report of serious adverse event occurring during clinical trial to a subject of clinical trial, shall, after due analysis, be forwarded to the Central Licencing Authority, the chairperson of the Ethics Committee and the institute where the trial has been conducted within fourteen days of its occurrence as per Table 5 of the Third Schedule and in compliance with the procedures as specified in Chapter VI;

XI. In case of injury during clinical trial to the subject of such trial, complete medical management and compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of the receipt of order issued by Central Licencing Authority in accordance with the provisions of the said Chapter;

XII. In case of clinical trial related death or permanent disability of any subject of such trial during the trial, compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of receipt of the order issued by the Central Licencing Authority in accordance with the provisions of the said Chapter;

XIII. The premises of the sponsor including his representatives and clinical trial sites, shall be open for inspection by officers of the Central Licencing Authority who may be accompanied by officers of the State Licencing Authority or outside experts as authorised by the Central Licencing Authority, to verify compliance of the requirements of these rules and Good Clinical Practices Guidelines, to inspect, search and seize any record, result, document, investigational product, related to clinical trial and furnish reply to query raised by the said officer in relation to clinical trial;

XIV. Where the new drug or investigational new drug is found to be useful in clinical development, the sponsor shall submit an application to the Central Licencing Authority for permission to import or manufacture for sale or for distribution of new drug in India, in accordance with Chapter X of these rules, unless otherwise justified;

XV. The laboratory owned by any person or a company or any other legal entity and utilised by that person to whom permission for clinical trial has been granted used for research and development, shall be deemed to be registered with the Central Licensing Authority and may be used for test or analysis of any drug for and on behalf of Central Licensing Authority;

XVI. The Central Licencing Authority may, if considered necessary, impose any other condition in writing with justification, in respect of specific clinical trials, regarding the objective, design, subject population, subject eligibility, assessment, conduct and treatment of such specific clinical trial;

XVII. The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.

XVIII. The formulation intended to be used in the clinical trial study shall be manufactured under GMP conditions using validated procedures.

XIX. It may kindly be noted that merely granting permission to conduct Clinical trials/Bioavailability or Bioequivalence study with the drug does not convey or imply that, based on the Clinical trial data/ Bioavailability or Bioequivalence study data generated with the drug, permission to market this drug in the country will automatically be granted to you.

XX. **The result of the BE study shall be presented to the SEC committee before initiation of the CT study.**

FORM CT-06

(See rules 22, 25, 26, 29 and 30)

PERMISSION TO CONDUCT CLINICAL TRIAL OF NEW DRUG OR INVESTIGATIONAL NEW DRUG

Permission no.: FDC-CT-06-39/2023

1. The Central Licencing Authority hereby permits **M/s. Exemed Pharmaceuticals, Plot No. 133/1 & 133/2, G.I.D.C., Selvas Road, Vapi-396195, Gujarat Telephone No. 912606617700, Fax no. 912606617799** (Name and full address with contact details of the applicant) to conduct clinical trial of the new drug or investigational new drug as per protocol number **(Vide protocol no. CT/2023/11, version no. 01, dated 28.04.2023)** in the below mentioned clinical trial sites.
2. Details of new drug or investigational new drug and clinical trial site [As per Annexure].
3. This permission is subject to the conditions prescribed in part A of Chapter V of the New Drugs and Clinical Trials Rules, 2019 under the Drugs and Cosmetics Act, 1940.

Place: New Delhi

Date: .....

28 AUG 2023

Central Licencing Authority

Stamp

Dr. RAJEEV SINGH RAGHUVANSHI
Drugs Controller General (India)
Central Drugs Standard Control Organisation
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India
FDA Bhawan, Kotla Road,
New Delhi (India)

Annexure:

Details of new drug or investigational new drug:

Names of the new drug or investigational new drug:	Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin 10mg + Metoprolol Succinate IP eq. to Metoprolol Tartrate (Extended Release) 50mg tablets
Therapeutic class:	Antihypertensive and Antidiabetic
Dosage form:	Tablets
Composition:	Each film coated tablet contains: Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin ..... 10mg Metoprolol Succinate IP eq. to Metoprolol Tartrate (Extended Release) 50mg
Indications:	It is indicated in patients with heart failure Post-Acute Myocardial Infarction

Details of clinical trial site:

Names and address of clinical trial site:	As per annexure- A
Ethics committee details:	As per annexure- A
Name of principal investigator:	As per annexure- A

Annexure-A

Permission no.: FDC-CT-06-39/2023

S. No.	Name of PI	Site Name	Ethics Committee Name, Address & EC registration No.
1.	Dr. Sanjay Kumar Sharma	Maharaja Agrasen Superspeciality Hospital, Central Spine, Agrasen Aspatal Marg, Sector 7, Vidyadhar Nagar, Jaipur-302039, Rajasthan.	Institutional Ethics Committee, Maharaja Agrasen Superspeciality Hospital, Central Spine, Agrasen Aspatal Marg, Sector 7, Vidyadhar Nagar, Jaipur-302039, Rajasthan. ECR/1222/Inst/RJ/2019/RR-22
2.	Dr. Ashish Kumar Agarwal	Department of Cardiology, Jawahar Lal Nehru (J.L.N) Medical College, Kala Bagh, Ajmer-305001, Rajasthan.	Institutional Ethics Committee, Jawahar Lal Nehru Medical College, Kala Bagh, Ajmer-305001, Rajasthan. ECR/1156/Inst/RJ/2018/RR-22
3.	Dr. Mahmodullah Razi	LPS Institute of Cardiology, GSVM Medical College, Swaroop Nagar, Kanpur-208002, Uttar Pradesh.	Ethics Committee, GSVM Medical College, Room No-125, 1st Floor, Swaroop Nagar, Kanpur-208002, Uttar Pradesh. ECR/680/Inst/UP/2014/RR-20
4.	Dr. Kunal Sahai	Chandani Hospital Pvt. Ltd., 9/60, Arya Nagar Road, Khalasi Line, Arya Nagar, Kanpur-208002, Uttar Pradesh.	Institutional Ethics Committee, Chandani Hospital Pvt. Ltd., 9/60, Arya Nagar, Kanpur-208002, Uttar Pradesh. ECR/1249/Inst/UP/2019
5.	Dr. Rajesh Kumar Pandey	Chirayu Hospital, (A Unit of KSCH Pvt. Ltd), Kalwar Road, Hathoj, Jaipur-302012, Rajasthan.	Institutional Ethics Committee, Chirayu Hospital, (A Unit of KSCH Pvt. Ltd), Kalwar Road, Hathoj, Jaipur-302012, Rajasthan. ECR/1582/Inst/RJ/2021
6.	Dr. Sanjeev Chaudhary	W Pratiksha Hospital, Golf Course Ext. Road, Sushant Lok II, Sector 56, Gurugram-122011, Haryana.	North East Healthcare Private Limited, Golf Course Ext. Road, Sushant Lok-II, Sector 56, Gurugram-122011, Haryana. ECR/1282/Inst/HR/2019
7.	Dr. Bhagya Narayan Pandit	Dr. Ram Manohar Lohia Hospital, Postgraduate Institute of Medical Education and Research, Baba Kharak Singh Road, Near Gurudwara Bangla Sahib, Type III, Connaught Place, New Delhi-110001.	Ethics Committee, PGIMER, Dr. Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, Near Gurudwara Bangla Sahib, Type III, Connaught Place, New Delhi-110001. ECR/78/Inst/DL/2013/RR-19
8.	Dr. Mahesh Pandey	Vidhya Hospitals & Trauma Centre, Harikansgadi, Mohanlalganj, Raebareli Road, Lucknow-226301, Uttar Pradesh.	Vidhya Hospital and Trauma Centre Ethics Committee, Vidhya Hospitals & Trauma Centre, Harikansgadi, Mohanlalganj, Raebareli Road, Lucknow-226301, Uttar Pradesh. ECR/1579/Inst/UP/2021
9.	Dr. Biswarup Sarkar	Medical College, Kolkata, MCH Building, 4th Floor, 88 College Street, Kolkata-700073, West Bengal.	Institutional Ethics Committee for Human Research, Medical College and Hospital, Kolkata, 88, College Street, Kolkata-700073, West Bengal. ECR/287/Inst/WB/2013/RR-19

10.	Dr. Swapan Kumar Halder	Nil Ratan Sarkar Medical College and Hospital, Kolkata, 138, Acharya Jagadish Chandra Bose Road, Sealdah, Raja Bazar, Kolkata-700014, West Bengal.	Ethics Committee, Nil Ratan Sarkar Medical College and Hospital, 138, Acharya Jagadish Chandra Bose Road, Sealdah, Raja Bazar, Kolkata-700014, West Bengal. ECR/609/Inst/WB/2014/RR-20
11.	Dr. Tanmoy Majee	Ruby General Hospital Ltd., 576, Anandapur, Kasba, EM Bypass, Kolkata-700107, West Bengal.	Institutional Ethics Committee, Ruby General Hospital, 576, Anandapur, Kasba, Golpark, EM Bypass, Kolkata-700107, West Bengal. ECR/1202/Inst/WB/2019/RR-22
12.	Dr. Debasish Das	Department of Cardiology, 2nd Floor, All India Institute of Medical Sciences, Sijua, Patrapada, Bhubaneswar-751019, Odisha.	Institutional Ethics Committee, All India Institute of Medical Sciences, Sijua, P/O Patrapada, Bhubaneswar-751019, Khordha, Odisha. ECR/534/Inst/OD/2014/RR-20
13.	Dr. Sanjay Vithalrao Desai	Prakash Institute of Medical Sciences & Research (PIMS&R), Urun-Islampur, Islampur-Sangali Road, Islampur, Tal-Walwa, Dist-Sangali-415409, Maharashtra.	Prakash Medical College Institutional Ethics Committee, Prakash Institute of Medical Sciences & Research (PIMS&R), Urun-Islampur, Islampur-Sangali Road, Islampur, Tal-Walwa, Dist-Sangali-415409, Maharashtra. ECR/1052/Inst/MH/2018/RR-21
14.	Dr. Kulin Sheth	Aatman Hospital, 5, Anveshan Row House, Bopal Gam BRTS, Bopal-Ghuma Road, Bopal, Ahmedabad-380058, Gujarat.	Institutional Ethics Committee, Aatman Hospital, 5, Anveshan Row House, Opp. Umiya Mata Mandir, Bopal-Ghuma Main Road, Bopal, Ahmedabad-380058, Gujarat. ECR/1565/Inst/GJ/2021
15.	Dr. Bhosale Kartik Hanumant	Medipoint Hospitals Pvt. Ltd., 241/1, New D.P. Road, Aundh, Pune-411007, Maharashtra.	Penta-Med Ethics Committee, Medipoint Hospitals Pvt. Ltd., 241/1, New D.P. Road, Near Sai Heritage, Aundh, Pune-411007, Maharashtra. ECR/357/Inst/MH/2013/RR-20
16.	Dr. Chandrakant S. Upadhyay	Imperial Multispeciality Hospitals, Pingle Pride, Nr. Radha Swami Ashram, Chikhali, Pune-411062, Maharashtra.	Imperial Ethics Committee, Imperial Multispeciality Hospitals, Pingle Pride, Nr. Radha Swami Ashram, Chikhali, Pune-411062, Maharashtra. ECR/1693/Inst/MH/2022
17.	Dr. Yogesh Vinodbhai Solanki	Shree Pragati Foundation's Hira Mongi Navneet Hospital, Valji Ladha Road, Near Kalidas Natya Gruh, Mulund West, Mumbai-400080, Maharashtra.	Institutional Ethics Committee, Hira Mongi Navneet Hospital, Shree Pragati Foundation's Hira Mongi Navneet Hospital, Valji Ladha Road, Near Kalidas Natya Gruh, Mulund West, Mumbai-400080, Maharashtra. ECR/1793/Inst/MH/2023
18.	Dr. Satish Suryavanshi	SMC Heart Institute and IVF Research Centre, Infront of BSNL Office, Vidhan Sabha Road, Near Ashoka Ratan, Khamardih, Raipur-492007, Chhattisgarh.	SMC Heart Institute Institutional Ethics Committee, SMC Heart Institute and IVF Research Centre, Infront of BSNL Office, Vidhan Sabha Road, Near Ashoka Ratan, Khamardih, Raipur-492007, Chhattisgarh. ECR/1522/Inst/CG/2021

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19.	Dr. Gadepalli Ramesh	Yashoda Hospitals, Behind Hari Hara Kala Bhawan, S P Road, Secunderabad-500003, Telangana.	Yashoda Academy of Medical Education and Research, Yashoda Hospitals, Behind Hari Hara Kala Bhawan, S P Road, Secunderabad-500003, Telangana. ECR/49/Inst/AP/2013/RR-22
20.	Dr. Krishna Mala Konda Reddy P	Department of Cardiology, Osmania Medical College & General Hospital, Afzalgunj, Hyderabad, Telangana-500012.	Upgraded Department of Pathology, Osmania Medical College & General Hospital, Afzalgunj, Hyderabad, Telangana-500012, India. Or Ampath Central Reference Laboratory, Nallagandla, Serilingampally, Hyderabad-500019, Telangana. ECR/300/Inst/AP/2013/RR-19
21.	Dr. Jenny Madhuri Gudivada	Department of Cardiology, King George Hospital, Andhra Medical College, Maharanipeta, Visakhapatnam-530002, Andhra Pradesh.	Institutional Ethics Committee, King George Hospital, Maharanipeta, Collector Office Junction, Visakhapatnam-530002, Andhra Pradesh. ECR/197/Inst/KGH/2013/RR-20

Place: New Delhi

Date: .....

25 AUG 2023

Central Licencing Authority

Stamp

Dr. RAJEEV SINGH RAGHUVANSHI
Drugs Controller General (India)
Central Drugs Standard Control Organisation
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India
FDA Bhawan, Kotla Road,
New Delhi (India)

S. No	File Name & Drug Name, Strength	Firm Name	Recommendations
	salt complex 50mg (24mg and 26mg), 100mg (49mg and 51mg) &200mg (97mg and 103mg) tablet		
4.	FDC/MA/23/000288 Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin + Bisoprolol Fumarate IP (10mg+1.25mg, 10mg+2.5mg, 10mg+5mg & 10mg+10mg) tablet	M/s. Exemed Pharmaceutical	The firm did not turn up for presentation.
5.	FDC/MA/19/000106 Efonidipine Hydrochloride Ethanolate +Telmisartan IP (20mg+40mg/ 40mg+40mg) uncoated bilayered tablets	M/s. Zuventus Healthcare Ltd.	In light of the condition mentioned in permission in Form CT-23 dated 30.12.2021, the firm presented the Phase IV clinical trial protocol for FDC of Efonidipine Hydrochloride Ethanolate 40mg + Telmisartan IP 40 mg tablets before the committee. After detailed deliberation, the committee recommended for conduct of the Phase IV clinical trial. The firm should submit the Phase IV clinical trial report to CDSCO for further review by the committee.
6.	FDC/MA/20/000077 Azelnidipine + Metoprolol (SR) 8mg/8mg/16mg/16mg + 25mg/ 50mg/25mg/50mg tablet	M/s. Akums Drugs & Pharmaceuticals Ltd.	In light of the SEC recommendation dated 07.06.2023, the firm presented their proposal along with clarification/justification w.r.t. clinical trial result. After detailed deliberation, the committee opined that the firm should submit raw data of the CT to CDSCO for review by the committee.
7.	FDC/MA/23/000063 Dapagliflozin Propanediol monohydrate 5mg/5mg/10mg/10mg + Metoprolol Succinate IP eq. to	M/s. Exemed Pharmaceuticals	In light of the SEC recommendation dated 06.07.2023 & 07.07.2023, the firm presented their proposal along with BE report & revised Phase III clinical trial protocol with change in indication before the committee. The committee noted that CDSCO has already issued BE & CT NOC on 25.08.2023. However firm has not

S. No	File Name & Drug Name, Strength	Firm Name	Recommendations
	Metoprolol tartrate (ER) 25mg/50mg/25mg/50 mg tablets		initiated Phase III CT study. After detailed deliberation, the committee considered BE report and recommended for grant of permission to initiate the Phase III CT with the condition that Guideline Directed Medical Therapy (GDMT) for heart failure as a concomitant medication to be allowed for all the subjects. Accordingly, the firm should submit Phase III CT study report to CDSCO for review by the committee.
8.	FDC/MA/23/000293 Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin + Telmisartan (10mg+40mg/ 10mg+80mg) film coated tablet	M/s. Eris Lifesciences Limited	The firm presented their proposal along with BE study protocol & Phase III clinical trial protocol before the committee. After detailed deliberation, the committee recommended for grant of permission to conduct the BE study & Phase III clinical trial. The result of the BE study should be presented for review by SEC before initiation of the Phase III clinical trial.
Medical Device Division			
9.	CI/MD/2021/50669 Pericardial Bioprosthesis Dafodil (1st Brand), Dafodil Neo (2nd Brand), Flomeo (3rd Brand), Freesia (4th Brand)	M/s. Meril Life Sciences Private Limited	The firm presented the 100 patients data as recommended by the SEC (cardiovascular & Renal) dated 08.02.2023 After detailed deliberation, the committee recommended to present the data in the SEC meeting alongwith (cardiothoracic) surgeon.